Comments of Jennifer Jinot, U.S. Environmental Protection Agency.

Comment 1:

It's not clear from table 1.2 or from the text in chapter 1 (e.g., 2nd sentence of 3rd paragraph of section 1.0: "Table 1.2 presents estimates of impacts form some of the health effects associated with ETS exposure, and predictions of the numbers of *people* potentially affected in California,..." [emphasis added]) what the target population of the assessment is. I assume that it is nonsmokers, but active smokers are also affected by ETS. And how are nonsmokers defined? Are the population risk estimates for never-smokers only, or do they include long-term former smokers?

Response:

The definition of nonsmoker is somewhat study-dependent and ranges from never smoked at all to never regularly smoked more than 100 cigarettes in the subject's lifetime, to not smoking in the previous two weeks. For the endpoints associated with pregnancy, LBW and PTD, and for cardiac death and lung cancer death, the target populations are nonsmokers. Ex-smokers are not excluded. Estimates for the childhood endpoints, asthma, otitis media and SIDS, include only never-smokers. We have clarified this in the text.

Comment 2:

Also in Table 1.2, the attributable risk estimates are presented with too many significant figures. This gives an undue impression of greater precision than there really is.

Response:

Those estimates have been rounded to better reflect their precision.

Comment 3:

With respect to the actual estimates in Table 1.2, I found the derivations of the OM and SIDS estimates, but I wasn't able to find the derivations of the LBW, PTD, or asthma estimates. If

they're not in the assessment, they probably should be, because people are going to be citing the estimates, and some folks will want to know how they were derived.

Response:

The text has been amended to show how the estimates in Table 1.2 were derived. PTD has been deleted since we only present estimates for the health effects we consider causal.

Comment 4:

On page 1-10, in the paragraph immediately above Table 1.2, the 3rd sentence doesn't really follow from the 2nd. I think that the intention of the paragraph is to say something more like:

> "With regard to addressing biological plausibility for ETS effects based on active smoking data, analyses based on particular biomarkers should be considered with caution. Presumption of a linear dose-response between an effect and tobacco smoke exposure from either active smoking or ETS exposure as indicated by biomarker measurements ~~and effect~~ can be problematic. The ratios of constituents in mainstream smoke and ETS differ~~s~~, ..."

Response:

The commentator's suggested wording adds clarity and has been incorporated.

Comment 5:

Finally, in the references to chap. 1, there is a Taylor and Tweedie (1997) reference that says it's "in press". surely, that's been published by now if it's ever going to be?

Response:

The references have been amended to reflect the study's publication in Environmetrics 8(4): 351-372.

Comment 6:

It seems that subsections 3.1.2 and 3.1.3, which have to do with ETS *exposure* assessment, should be in their own section rather than part of Section 3.1, which is on mechanisms of injury.

Response:

Thank you for your suggestions; however, we note that there is an entire second document on exposure assessment so we have left the organization as is..

Comment 7:

At the beginning of Section 3.2.1, it would be helpful to have standard definitions for some of those effects, i.e., LBW, SGA, etc.

Response:

These definitions have been added.

Comment 8:

Some of the entries in Table 3.1 aren't consistent in reporting the "n"s for nonsmokers, but the results presented are for nonsmokers, so it would be helpful to have all the numbers consistently referring to nonsmokers.

e.g., Ahluwalia et la. n=13,497 for nonsmokers according to the text

Response:

Table 3.1 has been modified to indicate the "n" for non-smokers where appropriate.

Comment 9:

Also some of the "n"s aren't consistent across the various tables and text in chapter 3. I know that sometimes the original n isn't the same as the n with all the data necessary for analysis, but unless it's explained in the text what the various n's correspond to, the document should consistently use just the most relevant value.

E.g., for Dejmek et al., Table 3.1 reports n=8,624, but the text (p. 3-30) and Table 3.3 refer to 6,866 mother-infant pairs without any reference to an n of 8624, and of these, 4,309 were reportedly nonsmokers prior to conception. but then Table 3.3 refers to 3710 + 1797 maternal nonsmokers (w/ and w/o ETS), which adds up to 5507, which is close to the 4309 + the smokers who quit in the 1st and 2nd trimester (734 + 467) = 5510. but none of this is clear. and the results presented in Table 3.1 are for the nonsmokers specifically, not for n=8624 or n=6866.

Response:

The numbers reported in the tables and text have been verified with the original papers and the inconsistencies eliminated. Where it adds clarity, labels have been added to identify to what the "n" refers.

Comment 10:

In the Jedrychowski & Flak study, I got the impression that the cotinine levels were just used for the validation part of the study. So the results presented in Table 3.1 are for self-reported exposure, right? So I would omit the comment that the cotinine cutoff would mix light and non-smokers, because it makes it appear as if that mixing would be reflected in the reported results, but i don't think that's correct.

Response:

OEHHA agrees with the commentator's interpretation and the text mentioning the cotinine cutoff has been removed from the table.

Comment 11:

Also, on page 3-15 about the validation part of the study, the cutoff was used to separate smokers and nonsmokers, so the sentence "Nevertheless, based on the 25 ng/mL criterion, the authors found a significant misclassification (false negative) rate of 57% of ETS-exposed women as non-exposed" didn't make sense to me.

Response:

The commentator's confusion is understandable as the authors used a non-standard definition of misclassification. The text has been reworded and expanded as follows to add clarity. "Nevertheless, based on the 25 ng/ml criterion, the authors found a significant misclassification (false negative) rate of 57% reflecting women with plasma cotinine >25 ng/ml who claimed to be never or ex-smokers. Among the 142 women claiming to be never or ex-smokers, 5.6% had plasma cotinine above 25 ng/ml. Adjustment of the ORs for misclassification would raise the risk estimates."

Comment 12:

With respect to the Kukla et al. study, the text (p.3-28) says that babies of mothers passively exposed to > 15 CPD had a mean BW 49 g lighter, but Tables 3.1 and 3.3 say the decrease was 74 g. Also there appears to be a typo in Table 3.3 - according to the text and Table 3.1 MNS w/ETS should be 1178 not 1378.

Response:

The BW decrement in the text (49 g) is correct and the tables have been corrected. 1178 is the correct number and the table has been changed.

Comment 13:

In the first sentence of the discussion of Windham et al. (1999) on p. 3-22, i believe that it should read "992 *non*-smokers" not "992 smokers".

Response:

The commentator is correct and the text has been changed.

Comment 14:

2nd-to-last sentence on p. 3-29: I believe that should read "mothers' cotinine levels were above 1 ng/mL, ..."

Response:

The commentator is correct, however, that study has been replaced with a newer one by the same group.

Comment 15:

On p. 3-43, 4th sentence on Chatenoud et al. study: i think that should be: "The OR for SAB associated with ~~parental~~ paternal smoking..."

Response:

The commentator is correct and the text has been changed.

Comment 16:

p. 3-48, 2nd sentence: "But... the risk of a cleft for a fetus of a maternal non-smoker was similar to that of babies who carry the A2 allele and ~~maternal smokers~~ whose mothers were smokers ~~babies carry the A2 allele~~."

Response:

The commentator's suggested wording is clearer and has been incorporated.

Comment 17:

p. 4-24, section 4.3.2, 2nd sentence: "However ... children persistently exposed to ~~passive smoke~~ ETS..." [exposure can be passive but not the smoke] similarly, on p. 4-25, 1st sentence of Dollberg et al. discussion, and first line of p. 4-26.

Response:

Good point. The text has been changed.

Comment 18:

The conclusions on asthma induction in children and on asthma induction and exacerbation in adults in this draft are stronger than those in the 2000 National Academy of Sciences report on asthma. i would like to see some discussion of how the current evidence or CalEPA's interpretation of the evidence are different from that 2000 report.

Response:

Regarding the health impacts of ETS exposure on asthma, the National Academy of Sciences concluded in their 2000 report on asthma (NAS, 2000) that the evidence indicates a causal relationship between ETS exposure and asthma exacerbation in preschool-aged children. OEHHA agrees with this assessment.

The report further stated that there is an association between ETS exposure and the development of asthma in younger children but it stopped short of claiming that the association is causal.

Based on several studies, many of which have been published since the NAS report, OEHHA finds that the evidence does support a causal association between ETS and asthma induction in children. Among children examined in NHANES-III by Gergen et al. (1998) and Mannino et al. (2001), the highest risk for asthma was associated with the highest ETS exposures. The study by Mannino et al. was noteworthy in that ETS exposure levels were biochemically verified by serum cotinine measures, the highest of which were associated with the greatest risk for ever or current asthma.

For older children and adults, the NAS report concluded that there is limited or suggestive evidence of an association between chronic ETS exposure and exacerbations of asthma. Regarding the development of asthma in school-aged children, the report concluded that the data are insufficient to establish an association with ETS exposure. As mentioned in this update, there is no "gold standard" for defining asthma in epidemiological research. However, as indicated by Toren et al. (1993), respondents' reports of respiratory symptoms, especially wheezing, may have a greater sensitivity for identifying adults with asthma than reliance strictly on self-reported asthma. Wheezing, in particular, correlates with the criterion of bronchial hyper-responsiveness (Burney et al., 1989). Several studies described in this update found an association between ETS exposure and asthma or wheezing in adolescents (Withers et al. 1998) and in adults (Hu et al., 1997b; Irabarren et al., 2001; Janson et al., 2001; Kunzli et al., 2000; McDonnell et al., 1999). Collectively these studies support a causal association of asthma with chronic ETS exposure.

Comment 19:

I found the discussion of ETS and cystic fibrosis in CalEPA's 1997 ETS report very interesting. I didn't find cystic fibrosis mentioned in this draft at all. Is there no new evidence one way or the other on ETS and cystic fibrosis?

Response:

Two new studies have been summarized and added to the document. A small study by Beydon et al. (2002) found that ETS exposure exacerbates airway occlusion in children with cystic fibrosis. A larger study by Smyth et al (2001) found no effect of ETS exposure on lung function among children with cystic fibrosis. These new studies do not alter the original conclusion that the effects of ETS in cystic fibrosis are uncertain.

Comment 20:

In Section 6.2.3. it seemed that there were several new studies with strong evidence on lung development in children. I would have expected the updated findings (e.g., Table 6.00) to at least be "Suggestive (strengthened)".

Response:

Upon reflection, OEHHA agrees. The table has been changed.

Comment 21:

In Table 6.01, p. 6-4, re: the Li et al. study. the comments say that "In utero exposure strongly associated with decreased pulmonary function *especially if combined with postnatal ETS ...* [emphasis added]". However, most of the decreases in function listed seem to be of *lower* magnitude for "in utero + postnatal" vs. for "in utero" alone.

Response:

The sentence in question referred to FEV1 measures in boys. The table has been modified to clarify this.

Comment 22:

In Table 6.03, p. 6-15, under the Jindal et al. findings, it should read "1.7 vs. 6.1 p<0.01", i.e., the "1.7" is missing.

Response:

The 1.7 has been re-inserted.

Comment 23:

In Table 6.04, p. 6-20, under Li et al. outcome, where it says “overall”, the presented OR is for hospitalizations. it appears, though, that it is overall across the age groups since listed below are different age groups, but the age group ORs are for LRIs and the “overall” OR is for hospitalizations.

Response:

The commenter is correct and the table has been altered to clarify this point.

Comment 24:

In Table 6.04, p. 6-22, under Peters et al. study description, it says “1.5 - 13 yr-olds”; however, in the text (p. 6-31) it says that the 10,402 children are “ages 8 - 13 years”.

Response:

The text is correct and the table has been changed.

Comment 25:

In Table 6.12, p. 6-49, under Willes et al. exposure, the “15" in “15 ppm” got split across two lines.

Response:

They have been re-united

Comment 26:

In Table 6.13, p. 6-57, under Mannino et al. study description, it specifies 4-6 yr olds, and the results are the results for 4-6 y.o.’s, but the N = 13,944 isn’t just for the 4-6 y.o.’s, so it could be confusing the way it’s presented.

Response:

The number 13,944 includes all children in the study. The numbers for each age group, including 4-6 y.o, have been added to the table.

Comment 27:

In Table 6.13, p. 6-57, under Gergen et al. study description, the “2" is missing from “2 mo. - 5 yr”

Response:

The “2” has been added.

Comment 28:

In Table 6.13, p. 6-59, under Beckett et al. study description, it says “< 19 yr”, but in the text (p. 6-67) it says “less than 18 years”

Response:

The text is correct and the table has been changed.

Comment 29:

On p. 6-88, in Table 6.17, under Jaakola et al. study description, it says “18-40 yr old” but in the text on same page its says “aged 15-40".

Response:

The text is correct and the table has been changed.

Comment 30:

On p. 6-89, the 3rd paragraph begins “*Dubus et al. (1998)*”. I think that that should be Abbey et al.

Response:

The commentator is correct and the text has been changed.

Comment 31:

On p. 6-90, the 2nd paragraph begins “Emmons et al. (1996)”. I think that that one should be Berglund et al. (1999).

Response:

The commentator is correct and the text has been changed

References used in responses:

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Gergen PJ, Fowler JA, Maurer KR, Davis WW, Overpeck MD (1998). The burden of environmental tobacco smoke exposure on the respiratory health of children 2 months through 5 years of age in the United States: Third National Health and Nutrition Examination Survey, 1988 to 1994. Pediatrics 101(2):E8.

Hu FB, Persky V, Flay BR, Zelli A, Cooksey J, Richardson J (1997b). Prevalence of asthma and wheezing in public schoolchildren: association with maternal smoking during pregnancy. Ann Allergy Asthma Immunol 79(1):80-4.

Iribarren C, Friedman GD, Klatsky AL, Eisner MD (2001). Exposure to environmental tobacco smoke: association with personal characteristics and self reported health conditions. J Epidemiol Community Health 55(10):721-8.

Janson C, Chinn S, Jarvis D, Zock JP, Toren K, Burney P (2001). Effect of passive smoking on respiratory symptoms, bronchial responsiveness, lung function, and total serum IgE in the European Community Respiratory Health Survey: a cross-sectional study. Lancet 358(9299):2103-9.

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Mannino DM, Moorman JE, Kingsley B, Rose D, Repace J (2001). Health effects related to environmental tobacco smoke exposure in children in the United States: data from the Third National Health and Nutrition Examination Survey. Arch Pediatr Adolesc Med 155(1):36-41.

McDonnell WF, Abbey DE, Nishino N, Lebowitz MD (1999). Long-term ambient ozone concentration and the incidence of asthma in nonsmoking adults: the AHSMOG Study. Environ Res 80(2 Pt 1):110-21.

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Smyth A, O'Hea U, Feyerabend C, Lewis S, Smyth R (2001). Trends in passive smoking in cystic fibrosis, 1993-1998. Pediatr Pulmonol 31(2):133-7.

Toren K, Brisman J, Jarvholm B (1993). Asthma and asthma-like symptoms in adults assessed by questionnaires. A literature review. Chest 104(2):600-8.

Withers NJ, Low L, Holgate ST, Clough JB (1998). The natural history of respiratory symptoms in a cohort of adolescents. Am J Respir Crit Care Med 158(2):352-7.